Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Original) A method for detecting a GPCR-binding partner complex comprising a GPCR and a GPCR binding partner, said method comprising:

(a) culturing a cell producing a first and a second polypeptide, wherein at least one of said first and said second polypeptides is a GPCR,

(b) lysing said cell;

(c) contacting said first polypeptide with a substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein the presence of said second polypeptide on said substrate is indicative of a GPCR-binding partner complex.

2. (Currently amended) The method of claim 1, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner. [[.]]

3. (Original) The method of claim 1, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

4. (Original) The method of claim 1, wherein at least one of said first and said second polypeptides is an orphan GPCR.

5. (Original) The method of claim 1, wherein at least one of said first and second polypeptides is a native GPCR.

6. (Canceled)

7. (Original) The method of claim 1, wherein both of said first and said second polypeptides are GPCRs.

8-11. (Canceled)

12. (Original) The method of claim 1, wherein at least one of said first and said second polypeptides is recombinant.

13-22. (Canceled)

23. (Original) The method of claim 1, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

24. (Currently amended) The method of ~~any one of claims 1-22~~ claim 1, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

25. (Original) A method for detecting a GPCR-binding partner complex comprising a GPCR and a GPCR binding partner, said method comprising:

(a) culturing a cell producing a first and a second polypeptide, wherein at least one of said first and said second polypeptides is a GPCR,

(b) lysing said cell;

(c) contacting said first polypeptide with an addressable substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate in an addressable manner; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein the presence of said second polypeptide on said substrate is indicative of a GPCR-binding partner complex.

26. (Original) The method of claim 25, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner.

27. (Original) The method of claim 25, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

28. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is an orphan GPCR.

29. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is a native GPCR.

30. (Canceled)

31. (Original) The method of claim 25, wherein both of said first and said second polypeptides are GPCRs.

32-35. (Canceled)

36. (Original) The method of claim 25, wherein at least one of said first and said second polypeptides is recombinant.

37-51. (Canceled)

52. (Currently amended) The method of claim ~~38 or claim 48~~ 25, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

53. (Currently amended) The method of ~~any one of claims 25-51~~ claim 25, wherein said method further comprises selecting prior to said culturing step (a) said first and said second

polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

54. (Currently amended) A method of identifying whether a candidate polypeptide is a binding partner for a GPCR, comprising the step of detecting a GPCR-binding partner complex comprising said candidate polypeptide and said GPCR according to the method of ~~any one of claims 1-53~~ claim 1 or claim 25, wherein detection of said complex is indicative of said candidate polypeptide being a binding partner of said GPCR.

55. (Original) A method for detecting a GPCR-binding partner complex, said method comprising:

(a) culturing a plurality of cells, each cell producing a first and a second polypeptide, wherein at least one of said first and said second polypeptides is a GPCR, and wherein each cell produces a different GPCR;

(b) lysing said cells;

(c) contacting said first polypeptide from each cell with an addressable substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate at an address specific for said cell; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein the presence of said second polypeptide at an address on said substrate is indicative of a GPCR-binding partner complex comprising said first polypeptide and said second polypeptides produced by the cell having said address.

56. (Original) The method of claim 55 wherein said plurality of cells is at least 2, at least 5, at least 10, at least 15, at least 20, at least 25, at least 50, or at least 100 cells.

57. (Original) The method of claim 55, wherein said first and said second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

58. (Original) The method of claim 55, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

59. (Original) A method for detecting a GPCR-binding partner complex, said method comprising:

(a) culturing a cell, said cell producing a first and a plurality of a second polypeptide, wherein each of said plurality of said second polypeptide is different and wherein at least one of said first and said plurality of said second polypeptide is a GPCR;

(b) lysing said cell;

(c) contacting said first polypeptide with a substrate having affinity for said first polypeptide, under conditions suitable for binding of said first polypeptide to said substrate; and

(d) detecting the presence of said second polypeptide on said substrate, wherein said detecting is direct;

wherein the presence of said second polypeptide on said substrate is indicative of at least one GPCR-binding partner complex comprising said first polypeptide and said second polypeptide.

60. (Original) The method of claim 59 wherein said GPCR-binding partner complex is detected, further comprising repeating steps (a) to (d) one or more times with subsets of said plurality of said second polypeptide, said subsets encompassing said plurality, until a GPCR-binding partner complex is detected from at least one cell producing a said first polypeptide and a single said second polypeptide.

61. (Original) The method of claim 59 wherein said plurality of said second polypeptides is at least 2, at least 5, at least 10, at least 15, at least 20, at least 25 said, at least 50, or at least 100 of second polypeptide.

62. (Canceled)

63. (Original) The method of claim 59, wherein said first and second polypeptides are endogenously co-expressed in at least one cell type, tissue, or tissue sub-region.

64. (Original) The method of claim 59, wherein said method further comprises selecting prior to said culturing step (a) said first and said second polypeptides wherein said first and said second polypeptides are coexpressed in a least one cell type, tissue or tissue sub-region.

65. (Currently amended) The method of ~~any one of claims 55-64~~ claim 55 or claim 59, wherein said first polypeptide is a GPCR and said second polypeptide is a GPCR binding partner.

66. (Currently amended) The method of ~~any one of claims 54-64~~ claim 55 or claim 59, wherein said first polypeptide is a GPCR binding partner and said second polypeptide is a GPCR.

67. (Currently amended) The method of ~~any one of claims 55-64~~ claim 55 or claim 59, wherein at least one of said first and said second polypeptides is an orphan GPCR.

68. (Currently amended) The method of ~~any one of claims 55-64~~ claim 55 or claim 59, wherein at least one of said first and said second polypeptide is a native GPCR.

69. (Canceled)

70. (Currently amended) The method of ~~any one of claims 55-64~~ claim 55 or claim 59, wherein both of said first and said second polypeptides are GPCRs.

71-74. (Canceled)

75. (Currently amended) The method of ~~any one of claims 55-64~~ claim 55 or claim 59, wherein at least one of said first and second polypeptides is recombinant.

76-85. (Canceled)

86. (Currently amended) A method for identifying whether a candidate agent modulates binding of a GPCR to a binding partner for the GPCR, said method comprising the step of determining whether there is a difference in the amount of a GPCR-binding partner complex comprising said GPCR and said binding partner detected according to [[a]] the method of ~~any one of claims 1-52~~ claim 1 or claim 25, wherein said difference is determined for contacting or not contacting said candidate agent with said first and said second polypeptides prior to said detecting step (d) of said method and wherein an alteration in said amount of said second polypeptide detected on said affinity substrate is indicative of an agent that modulates binding of said GPCR to said binding partner for the GPCR.

87. (Original) The method of claim 86, wherein said first and said second polypeptides are contacted with said candidate agent during step (a), step (b) or step (c).

88. (Original) The method of claim 86, wherein said candidate agent is a small molecule, a peptide, a ligand for said GPCR, or an antibody.

89. (Original) The method of claim 86, wherein said modulator reduces said binding of a GPCR to a binding partner for the GPCR by more than about 10%, more than about 20%, more than about 30%, more than about 40%, or more than about 50% as compared to said binding in the absence of said agent.

90. (Original) The method of claim 86, wherein said modulator increases said binding of a GPCR to a binding partner for the GPCR by more than about 10%, more than about 25%, more than about 50%, more than about 100%, more than about 200%, more than about 300%, more than about 400%, or more than about 500.

91. (Currently amended) The method according to any one of claims [[1-90]] 1, 25, 55 and 59 wherein said first and said second polypeptides are both mammalian.

92. (Currently amended) The method according to ~~claim 91~~ any one of claims 1, 25, 55 and 59 wherein said first and second polypeptides are both human.

93. (Original) A composition comprising an addressable affinity substrate, said addressable affinity substrate comprising a plurality of addresses having affinity for different GPCRs.

94-97. (Canceled)

98. (Original) A composition comprising a cell, said cell producing a first and a second polypeptide, wherein said first and said second polypeptides are a GPCR and a GPCR binding partner, and wherein said first polypeptide comprises an affinity tag and said second polypeptide is fused to a reporter protein.

99-115. (Canceled)

116. (Original) A composition comprising a library of GPCRs, wherein said library comprises a plurality of pairs of isolated polynucleotide wherein both a first and a second said polynucleotide of said pair comprises a first nucleotide sequence encoding the same GPCR, said encoded GPCR of one said pair being different from said encoded GPCR of any other said pair, and wherein said first polynucleotide of said pair further comprises a second nucleotide sequence encoding an in-frame affinity tag and said second polynucleotide of said pair further comprises a third nucleotide sequence encoding an in-frame reporter protein.

117. (Original) The composition of claim 116 wherein said affinity tag is an epitope tag and said reporter protein is luciferase.

118. (Original) The composition of claim 116 wherein said library comprises at least about 50 said pairs, at least about 100 said pairs, at least about 200 said pairs, at least about 300 said pairs, at least about 400 said pairs, or at least about 500 said pairs.

119. (Original) The composition of claim 116 wherein said encoded GPCR is native.

120. (Original) The composition of claim 116 wherein said encoded GPCR is mammalian.

121. (Currently amended) The composition of claim [[120]] 116 wherein said encoded GPCR is human.